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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/542,914 | 03/07/2006 | Alfred Marchal | 09997.0127USWO | 9556 |

23552 7590 12/05/2008

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| EXAMINER | |
|---|---|
| VALENROD, YEVGENY | |
| ART UNIT | PAPER NUMBER |
| 1621 | |
| MAIL DATE | DELIVERY MODE |
| 12/05/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/542,914 | MARCHAL, ALFRED | |
| | Examiner | Art Unit | |
| | YEVEGENY VALENROD | 1621 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 3-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

The following is a final office action in application # 10542914. This application has been transferred to Examiner Valenrod whose contact information is provided at the end of the instant document.

Amendment to the claims filed 7/28/08 is acknowledged.

Rejection of claims1 and 3 under 35 USC 112 first paragraph is withdrawn in view of applicants remarks. Specification on page 3, lines 24-31 provides a limited definition of what applicant believes to be covered by the term dermatological lesions and said lesions are known to be treated by vitamin K1 as evidenced by Elson et al at column 1, lines 24-31.

Rejection of claims 1 and 3-10 is maintained. The Text of the rejection is repeated below followed by reply to Applicants remarks.

***Claim Rejections – 35 USC 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

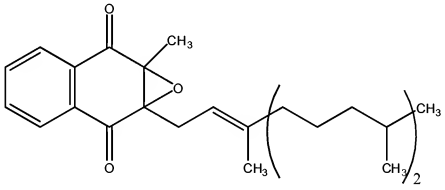
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-10 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Elson (U.S. Patent 5,510,391), in view of Ryall et al. (J. Med. Chem. 1990 (33), 1790-1797).

The instant claims are drawn to a method of treating dermatological lesions of a mammal by using a compound of formula I, as depicted below:




*Scope of prior art*

Elson teaches that synthetic Vitamin K1 analogs can be used in cosmetic and/or pharmaceutical formulation for use in treating the skin (see column 7, lines 18-20; abstract), as a cream (column 3, line 19-21) at concentrations of 1% and 5% (column 3,

lines 40 and 55). Vitamin K1 oxide would be considered to be a species of the generic teaching of Elson. Elson's formulations treats blood vessel disorders of the skin, including actinic and iatrogenic purpura, lentigines, telangiectasias of the face, spider angiomas, spider veins of the face, spider veins of the legs and other vascular problems of the skin and subcutaneous tissue (column 1, lines 24-31). Additionally, Elson's formulations contain lecithin granules which are composed of lipid particles (abstract).

Regarding claims 4, 5 and 8 which presents limitations as to the particle size of the phospholipids and the percentage of the compound of Formula 1, it is the position of the examiner that one of ordinary skill in the art, at the time of the invention, would through routine and normal experimentation determine the optimization of these limitations to provide the best effective variable depending on the results desired. Thus it would be obvious in the optimization process to optimize the particle size of the phospholipids and the percentage of the compounds. Note that the prior art provides the same effect desired by applicant, the treatment of the same skin conditions.

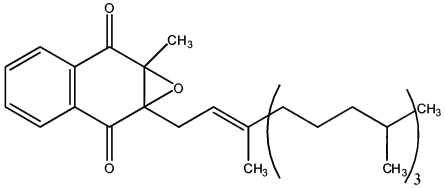
*Difference between prior art and instant claims*

Elson is deficient in that it does not explicitly teach Vitamin K1 epoxide analogs as instantly claimed.

*Secondary reference*

Ryall et al. teaches Vitamin K1 epoxide analogs, including a homolog to that of Applicant's, differing only by one repeating isoprene unit., as shown below (page 1791,

first column, compound 1, compound 2, second column, table 1, Vitamin K epoxide, first compound).



Additionally, Ryall et al.'s compounds are found to be inhibitors of Vitamin K1 epoxide reductase (page 1790, second column, first paragraph to page 1791, first column, first paragraph). The Examiner takes the position that it is reasonable to assume the mechanism of action for Applicant's Vitamin K1 epoxide compound also involves the inhibition of Vitamin K1 epoxide reductase, as taught by Ryall et al. Ryall et al. is analogous art because compounds of the same structural formula that differ only by one repeating unit would be obvious. Thus, varying Ryall et al.'s compounds by one homologous isoprene unit, would give rise to the compound of the instant claims. In the absence of unexpected results, one skilled in the art would expect that the instant claims, directed to a compound that is homologous to the compounds of Ryall et al. are prima facie obvious.

Therefore, it is the position of the examiner that one of ordinary skill in the art, at the time of the invention, would through routine and normal experimentation determine the

appropriate number of isoprene units in the side chain of the synthetic Vitamin K1 epoxide, as taught by Ryall et al. In addition, one of ordinary skill in the art would use these Vitamin K1 analogs in cosmetic and/or pharmaceutical formulation for use in treating the skin, as taught by Elson. Slight variations in the length of the side chain of Vitamin K1 epoxide suggests the compounds have similar properties and utilities. "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." (see MPEP § 2144.08c).

One of ordinary skill in the art would be motivated to use Ryall et al.'s compounds for Elson's formulations, with the reasonable expectation that the compounds would treat dermatological conditions involving blood vessel disorders, by inhibiting Vitamin K1 epoxide reductase. Furthermore, the limitations in some of the dependent claims, not expressly taught in the art, are also deemed to be obvious. One of ordinary skill in the art would be motivated to tweak and optimize these parameters to arrive at the instantly claimed invention. The expected result would be the efficient production of Applicant's synthetic Vitamin K1 epoxide analog for the pharmaceutical and cosmetic industry.

***Reply to applicants Remarks***

Applicant has traversed the obviousness rejection above on the following basis:

Applicant has argued that vitamin K1 of Elson and vitamin K1 oxide of Ryall are not analogues based on structural differences between the two.

Examiner disagrees with above argument. In the instant specification on page 2, lines 17-20, the art recognized equivalency in physiological activity of vitamin K1 and Vitamin K1 oxide is provided. One skilled in the art would therefore expect the compound on Vitamin K of Eller and Vitamin K1 oxide of Ryall to have the same physiological activity such as the treatment of dermatological lesions as described by Eller.

Applicant has cited *In re* Steminski (page 6 last line – page 7, line 9). Applicant has also contended that Ryall fails to provide a utility for the disclosed compounds.

Examiner disagrees with applicant's assertion. Ryall et al disclose the compounds to be inhibitors of Vitamin K1 epoxide reductase, which demonstrates biological activity of the compounds. The compounds are also linked by the instant specification to the vitamin K1 activity disclosed by Elson et al. Therefore, although Ryall et al do not disclose their compounds in treatment of dermatological lesions, it is known from prior art that they can in fact be used for such treatments. The treatment of dermatological lesions using the compound of the instant invention that comprises the core structural featured of the Ryall's compounds is therefore obvious.

One skilled in the art would expect the instant compound to have similar activity as Ryalls compound. Since Ryalls compound is expected to be useful in treatment of dermatological lesions based on the disclosure of Elson and knowledge in prior art that Elsons and Ryalls compounds have the same pharmacological activity, the instantly

claimed method of treatment is obvious. This rejection can be overcome by a showing of unexpected results arising from the difference in the number of repeating isoprene units in the structure of the instant compound or structurally related compound.

***Conclusion***

Claims 1 and 3-10 are pending

Claims 1 and 3-10 are finally rejected

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yevgeny Valenrod whose telephone number is 571-272-9049. The examiner can normally be reached on 8:30am-5:00pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel Sullivan can be reached on 571-272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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